

Abstracts

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that the FDA will evaluate PRO recall periods. This study reviews the literature around PRO recall periods in the light of the final guidance and provides recommendations to sponsors wishing to obtain FDA label claims on the basis of PRO endpoints. **METHODS:** A literature review was conducted in Embase and Medline, with further searching in Google scholar. References from each of the relevant papers were hand searched. Forty four papers were reviewed with reference to section D3 of the FDA final PRO guidance, the research was summarized and a set of recommendations were developed. **RESULTS:** Psychological literature identifies that recall of complex information is problematic e.g. limited and selective memory and systemic biases. The majority of empirical work with PROs focuses on the measurement of pain with some evidence from fatigue measurement. Whilst most studies focus on symptoms, others examine HRQL, adherence and treatment satisfaction. Empirical research suggests a lack of correlation between actual experienced symptoms and recalled symptoms, with variability in patient attention to the recall period instruction. Recall is significantly influenced by the concept being measured and attributes of the patient at the time of assessment. The findings from the research are in line with the FDA concerns and their preference for shorter recall periods. **CONCLUSIONS:** The final FDA PRO guidance takes a considered approach to PRO recall periods in light of available research. Recommendations are presented on how best to select and justify the most appropriate recall period for a PRO measure in order to support regulatory review of drug approval label claims.

PMC38

DETERMINING MISSING DATA RULES FOR PROS: ALPHA-IF-ITEM-DELETED

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Missing outcomes data in clinical trials can be detrimental to identifying important treatment effects because power is reduced and uncertainty is increased. Although missingness at the scale level for patient-reported outcomes (PROs) (e.g., due to attrition) is a considerable challenge to measurement in longitudinal clinical trials, missingness at the item level for PROs (e.g., due to omission) can be more easily overcome and a reliable scale score calculated. The FDA PRO Guidance states that the maximum tolerable number of missing item-level responses should be determined during the instrument development process, but no particular method is advocated, and instrument developers often recommend arbitrary guidelines. Although a number of methods exist for examining the effect of missing data on scale precision, one simple approach is to calculate Cronbach's coefficient alpha sequentially as each item is deleted from the item set. The order in which items are removed from the item set is based on deleting the item with the largest contribution to alpha (i.e., alpha-if-item-deleted). When Cronbach's alpha for the set of remaining items falls below an a priori identified threshold (e.g., 0.70), the number of items deleted from the scale minus one is the maximum number of responses that can be missing for a scale score to be reliably calculated for a subject. We explored this approach with several validated instruments and found that the developer's guidelines are often stricter than the alpha-if-item-deleted method. Broader application of the Cronbach's alpha approach would result in fewer missing PRO scale scores, increased statistical power, reduced uncertainty, and additional information with which to assess treatment effects.

PMC39

TAPPING INTO A NEW DATA COLLECTION PARADIGM: USING DIRECT TO PATIENT PROGRAMS FOR MORE COST EFFECTIVE STUDY MANAGEMENT

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OBJECTIVES: 1) Understand how to navigate the regulatory environment, manage patient safety profiles, and achieve optimal process effectiveness in designing a Direct to Patient study; 2) Gather information on leveraging integrated technologies to support these studies; and 3) Learn key challenges and solutions from early Direct to Patient study implementations **METHODS:** The presentation will outline how to best design Direct to Patient studies to collect the right patient outcome data that will drive the most useful analysis. The presentation will look at the use of patient reported data to drive enrollment at the IND stage. Various methods of collecting patient data directly will be reviewed. **RESULTS:** Many questions are arising as the industry embarks on Direct to Patient programs, including how to navigate the regulatory challenges and various controls and guidelines. Other issues include how to address the changing role of investigators in this study model. Optimal roadmaps for designing Direct to Patient studies will be discussed, including the implementation of a flexible clinical and medical infrastructure to monitor patient participation. Issues such as the shift from site management to patient management, the process for management from recruitment to retention, and the processes for adverse event follow-up will be discussed. The optimal use of technology, such as portals, Randomization and Trial Supply Management technologies and ePRO data collection tools as well as the use of EDC in Direct to Patient programs will be discussed along with the right application of web-based and new social media tools. **CONCLUSIONS:** The increased need to have more outcomes and effectiveness data along with mounting pressure on the biopharmaceutical industry to contain costs have forced companies to look at new ways to manage studies more effectively and efficiently. There is a trend toward designing studies that reach out to patients directly in new ways, while at the same time eliminating costs and intermediaries associated with traditional studies.

PMC40

INSTIGATING AND ENCOURAGING INDIVIDUAL HEALTH BEHAVIORS THROUGH TECHNOLOGY: A TRANSTHEORETICAL PROPOSITION

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OBJECTIVES: The purpose of this conceptual work is to propose a transtheoretical framework for the development, selection, and evaluation of consumer technologies that promote individual health behaviors. To the best of our knowledge, this work is the first of its kind to transcend the traditional "informatics/organizational interventions" dyad to suggest, instead, an alternative conceptualization of technology rooted in theories of individual health behaviors, and one that acknowledges personal agency as a key factor vis a vis consumer technology decisions within the health context. **CHALLENGE:** Consumer technologies represent a hitherto untapped opportunity for encouraging affirmative and beneficial health behaviors on the individual level. Advances in information technologies including ubiquitous computing, social networking, and broadband Internet access have increased the scope and availability of health-related information. However, empirical evidence implicates the abundance of information sources as culprits in the widening knowledge gap among subpopulations of consumers. The relegation of technology to the realm of information-only is equally problematic for its presumed bias against uses of technology in "non-informatics" contexts, and for its apparent ignorance of the role of consumers as agents of their own health behaviors. **RECOMMENDATION:** We propose the novel application of The Transtheoretical Model (TTM) of Behavior Change at the critical intersection of consumer technologies and individual health behaviors. As we discuss in our work, TTM accommodates a consumer-focused vision of technology that is cognizant of the multi-stage, multi-process, and non-linear nature of human action in the context of adopting and maintaining health behaviors. We conclude our work with a list of principles informed by TTM to guide the development, selection, and evaluation of new and innovative technologies that encourage the adoption and maintenance of health behaviors by individual consumers.

PMC41

PATIENT-REPORTED OUTCOMES IN CLINICAL RESEARCH: PRESENT STATUS AND A LOOK TO THE FUTURE

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A combination of factors have contributed to an increased interest in patient-reported outcome (PRO) data. Increased chronic diseases and aging population, empowered patient group, a shift of treatment focus from curing diseases to ameliorating symptoms, as well as increasing budget constraint and competition among drugs developers are among the factors driving an increasing interest in assessing PROs. As the number and quantity of PROs increase, quality and criteria to assess these measures as well as sources of error and bias are increasingly being emphasized. A series of efforts were made in EU and the US to propose criteria for evaluating the scientific quality of PRO data in clinical practice. At the same time, major organizations sought to rationalize the field and improve the standing of PRO assessments through open communications with key regulatory agencies including the FDA and the EMEA. Accordingly, issues related to methodological standards for measuring and interpreting PROs in the drug evaluation process were debated and the research agenda on PROs were expedited. Current major trends in PRO research include computerized adaptive testing (CAT), ePROs, and an integrated data collection. The adoption of CAT supported by modern psychometrics such as Item Response Theory (IRT) have the potential to achieve far greater precision in measuring health outcomes without increasing the response burden. However, crucial theoretical and methodological concerns need to be addressed before widely applying this approach in patient outcome research. ePROs have prevailed in clinical trials and shown high patient acceptance. The advantages of ePRO are evident. However, practical issues may be another hurdle before the practice is widely accepted in clinical research. Finally, as PRO data collection becomes more common in clinical trials, the coordination of integrated data collection may be of benefit to all stakeholders.

PMC42

EXAMINATION OF THE DIFFERENCES IN PATIENT SATISFACTION BETWEEN FIRST VISIT AND RETURN VISITS: ANALYSIS OF A USA SELF-REPORTED SURVEY DATA

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OBJECTIVES: Very few studies have attempted to document differences in patient satisfaction between first and return visits. Therefore, we examined the differences in patient satisfaction with their primary care physician at first visit compared to return visits. **METHODS:** We conducted a cross-sectional national web based survey study consisting of anonymous patients rating their physicians on the basis of treatment satisfaction received from their most recent outpatient visit. The user-friendly validated survey was designed to help patients identify their physicians as per specialties and rate them on a scale of 0 ("not at all satisfied") to 10 ("extremely satisfied"). The association between satisfaction with primary care physician and patient ratings of total care between first visit and return visits was accessed using robust regression analysis. **RESULTS:** A total of 9974 patients who rated physicians belonging to the categories of first visit and return visits were included in this study. Other things being equal, return visits have a sizable effect on patient satisfaction. For unit change from first to return visits the coefficient of patient satisfaction for the return visits was 10.5